amino acid sequence 17-36 and/or amino acid sequence 56-84; wherein said conjugated compound is taken up by said cell and localized to the nucleus of said cell.

REMARKS

Status of the Claims

The rejection of claims 1-11 under 35 U.S.C. §112, first paragraph, was withdrawn. Claims 1-11 remain rejected under 35 U.S.C. §102 and §103. Claims 1 and 7 have been amended. Upon entry of this response, claims 1-11 are pending.

Rejection under 35 U.S.C. § 102

Claims 1, 3, and 5-11 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by WO 96/08970 (the "Weiner reference"). The Office alleges that the Weiner reference disclosed "nucleic acid molecules [that] are conjugated to a 'Vpr protein or its fragment,'" and that the Weiner references, "does not place any limitation on the length of the Vpr fragment, and embraces a [V]pr fragment of 95 amino acid residues comprising residues 17-36 and/or 59-84 of Vpr protein as instantly claimed." Applicants respectfully disagree.

The standard for anticipation under 35 U.S.C. § 102(b) is one of strict identity. An anticipation rejection requires a showing that each limitation of a claim be found in a single reference, *Atlas Powder Co. v. E.I. DuPont de Nemours & Co.*, 224 U.S.P.Q. 409, 411 (Fed. Cir. 1984). Claims 1 as amended recites "a nuclear localization sequence fragment of HIV-1 Vpr comprising amino acid sequence 17-36 and/or amino acid sequence 59-84," and claim 7 as amended recites "a nuclear localization sequence fragment of HIV-1 Vpr protein comprising amino acid sequence 17-36 and/or amino acid sequence 56-84." Nowhere does the Weiner reference teach such a fragment of Vpr. Indeed, Applicants can only locate one portion of the Weiner reference that reports any particular fragments of Vpr protein—page 53, lines 13-17, where fragments comprising residues 27-39, 35-48, 41-55, 49-60, and 66-68 are reported. Significantly, none of these fragments reported in the Weiner reference are the fragments comprising amino acids 17-36 and/or 59-84 recited in Applicants' claims. Additionally, the Weiner reference does

not disclose or teach the nuclear localization sequences of Vpr. Thus, the Weiner reference does not anticipate Applicants' claimed invention.

The Office Action asserts that because claim 1 recites "comprises" the Weiner reference reads on the claim language. The claims expressly requires that amino acid sequence 17-36 and/or amino acid sequence 59-84 be present. The Weiner reference does not describe these specific fragments. The claims have been amended to more clearly demonstrate reflect this. As amended the claims also recite that the fragments comprising amino acid sequence 17-36 and/or amino acid sequence 59-84 have nuclear localization activity. The Weiner reference does not discuss Vpr fragments with nuclear localization activity comprising the specific fragments recited in the claims.

Additionally, it appears from the Office's arguments in the Advisory Action (mailed July 24, 2002) and the Office Action (mailed April 9, 2002), that the Office believes that the Weiner reference anticipates the present invention because it discloses fragment sizes that encompass the fragments that are claimed in the present application. However, the Weiner reference discloses a genus, while the fragments claimed in the present application a part of another genus in which some of the species of the claimed genus are species that fall within the genus in the Weiner reference. It is well settled that a genus does not necessarily anticipate a species or a subgenus (see MPEP 2131.02). Additionally, the MPEP states

> When the compound is not specifically named, but instead it is necessary to select portions of teachings within a reference and combine them, e.g., select various substituents from a list of alternatives given for placement at specific sites on a generic chemical formula to arrive at a specific composition, ***anticipation can only be found if the classes of substituents are sufficiently limited or well delineated***. (emphasis added, MPEP 2131.02)

In the present case, the fragment sizes discussed by the Weiner reference could be considered the list of alternatives available to the art-skilled. However, this list of alternatives is ***not*** sufficiently limited or well delineated. Vpr is a protein that normally consists of 96 amino acid residues. Therefore, if the art-skilled were to choose fragments that were 3-25 residues in length that person would have 1,909 fragments to choose from.

This is not sufficiently limited. The MPEP requires that a person of ordinary skill in the art to be able to "at once envisage" the specific compound within the genus. In this instance, a person of ordinary skill in the art, would not have been able to immediately envisage the residues that comprise the Vpr fragments that are claimed in claims 1-11 because the choices are not sufficiently limited or delineated.

Thus, the Weiner reference does not disclose each and every limitation of the claims and therefore, cannot anticipate the present invention. Therefore, Applicants respectfully request that the rejection under 35 U.S.C. § 102(b) be withdrawn.

Rejections under 35 U.S.C. § 103(a)

Claims 1-11 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over the Weiner reference in view of U.S. Patent 6,005,004 (hereinafter, the "Katz reference") or U.S. Patent 6,232,295. (hereinafter, the "Kayyem reference"). The Office and Advisory Actions mistakenly assert that it would have been *prima facie* obvious for one skilled in the art to modify the methods of the Weiner reference by adding polycationic peptide sequence taught by the Katz or Kayyem references. Applicants traverse the rejection and respectfully request reconsideration because even if the cited references are combined, the claimed invention would not be produced.

In the Advisory Action the Examiner states, "the [103] rejection would stand or fall together with the rejection under 35 U.S.C. § 102(b)." (Advisory Action, page 2) As discussed above, the Weiner reference does not anticipate the present invention. Furthermore, the Weiner reference cannot be used to render the present invention obvious because there is no suggestion or motivation to use the fragments that are claimed in the instant application. Without such suggestion or motivation, the *prima facie* argument put forth by the Examiner falls apart. The Weiner, Katz, and Kayyem references do not discuss the nuclear localization sequences of Vpr. There is no suggestion within any of the cited references to use any fragments of Vpr as nuclear localization sequences or as a method to transport a composition to the nucleus of the cell.

The Weiner reference does not disclose the fragments that are useful or those that would have biological properties that would be important to a person of ordinary skill in the art. Most of the fragments one would produced by using the Weiner reference would

not have the function that is claimed in the present application. The Weiner reference does not disclose the fragments that have amino acid 17-36 or 58-84 and have the nuclear localization activity nor does it suggest such fragments with the nuclear localization activity. It is only through the use of hindsight reconstruction that the Examiner is able to make the claimed invention by combining the references cited. However, this is strictly prohibited. However, even if the references are combined they do not produce the claimed inventions because the fragments with the amino acid sequences that are claimed in the present application are not discussed.

Therefore, there is no *prima facie* case of obviousness because there is no motivation to combine the references because none of the references suggest the combination or refer to the other references explicitly or implicitly and even if the combination were made the combination does not produce the Applicants invention.

Moreover, specific fragments of Vpr that are claimed are non-obvious because nothing in the cited art teaches or suggests that the specifically claimed fragments would possess the claimed function. The claims recite specific fragments of Vpr that have a nuclear localization sequence and activity, and in the case of claim 7 are part of a method of delivering a compound to the nucleus of a cell. The Weiner reference does not suggest or teach fragments that have nuclear localization activity comprising the amino acid fragments of Vpr that are claimed in the present Application. The Vpr fragments that are claimed in the present Application are not obvious.

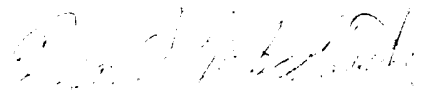
Accordingly, Applicants respectfully request the rejection under 35 U.S.C. § 103(a) be withdrawn.

Conclusion

Claims are in condition for allowance. An indication of allowability is therefore earnestly solicited. Applicant invites the Examiner to contact the undersigned at (215) 665-6928 to clarify any unresolved issues raised by this response.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned **"Version with markings to show changes made."**

Respectfully submitted,



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Version with markings to show changes made

In the Claims:

1. (Amended Thrice) A conjugated composition comprising a nuclear localization sequence fragment of HIV-1 Vpr comprising amino acid sequence 17-36 and/or amino acid sequence 59-84 conjugated to a therapeutic compound.

7. (Amended twice) A method of delivering a compound to the nucleus of a cell comprising the step of:

contacting said cell with a conjugated compound that is either said compound conjugated to a nuclear localization sequence fragment of HIV-1 Vpr protein comprising amino [acid] acid sequence 17-36 and/or amino acid sequence 56-84; wherein said conjugated compound is taken up by said cell and localized to the nucleus of said cell.